PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference P212500PCT	FOR FURTHER ACTION	See Form PCT/IPEA/416
International application No. PCT/NL2004/000910	International filing date *(day/month/year)* 24.12.2004	Priority date *(day/month/year)* 24.12.2003
International Patent Classification (IPC) or national classification and IPC INV. A61K31/197 A61P1/00		
Applicant N.V. NUTRICIA et al.		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 6 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ *sent to the applicant and to the International Bureau)* a total of sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the International application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in celectronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☐	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☒	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
24.10.2005	05.05.2006
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Allnutt, S Telephone No. +49 89 2399-7817

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/NL2004/000910

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3 and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4)
   - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages

1-20 as originally filed

Claims, Numbers

1-17 received on 24.10.2005 with letter of 24.10.2005

☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/NL2004/000910

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-17
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-17
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-17
	No:	Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (SEPARATE SHEET)

International application No.
PCT/NL2004/000910

1. The following documents are referred to in this communication; the numbering will be adhered to in the rest of the procedure:

D1: DE 43 04 394 A (FRESENIUS AG) 2 September 1993 (1993-09-02)
D2: US-B1-6 322 821 (REGISTER JACK W) 27 November 2001 (2001-11-27)
D3: US-B1-6 544 515 (BALLEVRE OLIVIER ET AL) 8 April 2003 (2003-04-08)
D4: DE 299 16 231 U (RENNER JOBST) 17 February 2000 (2000-02-17)
D5: DATABASE WPI Section Ch, Week 199349 Derwent Publications Ltd., London, GB; Class B05, AN 1993-392565 XP002272845 & JP 05 294833 A (TAKEDA CHEM IND LTD) 9 November 1993 (1993-11-09)
D6: PATENT ABSTRACTS OF JAPAN vol. 2000, no. 16, 8 May 2001 (2001-05-08) & JP 2001 008637 A (SHINKYO SANGYO KK), 16 January 2001 (2001-01-16)
D7: DATABASE HCA Accession Number :69:84590 ORLINSKII B: "The efficiency of pantothenic acid and vitamin B additions when fattening pigs on food wastes" XP002272844
D8: DATABASE WPI Section Ch, Week 199720 Derwent Publications Ltd., London, GB; Class B04, AN 1997-213412 XP002272846 & CN 1 097 563 A (CHEN Y) 25 January 1995 (1995-01-25)
D9: DATABASE BIOSIS [Online] BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 1990, ROEM A J ET AL: "VITAMIN REQUIREMENTS OF BLUE TILAPIAS IN A RECIRCULATING WATER SYSTEM" XP009027255 Database accession no. PREV199090060802
D10: US-A-6 036 984 (BURRI JOSEPH ET AL) 14 March 2000 (2000-03-14)
D11: US-B1-6 245 803 (REYNOLDS PATRICIA A ET AL) 12 June 2001 (2001-06-12)
D12: DATABASE EMBASE ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL; EMB-1996222979 1996, SMITH C M: SONG W: "Comparative nutrition of pantothenic acid" XP002224437

The documents considered in the present processing are consecutively numbered D1-D12; this numbering results from the citations D1-D12 found in the Search Report (SR) of the corresponding PCT application. It will be adhered to in the rest of the procedure. The cited passage(s) for each citation will be considered unless otherwise specified.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Novelty

1.The technical features of claims 1-17 are not anticipated by documents D1-12 and therefore fulfil the requirements of novelty in terms of Art 33 (2) PCT.
None of the prior art disclose compositions containing 14-1000mg pantothenic acid and protein, carbohydrates or lipid components such as those described in the claims.

Inventive Step

2. Claims 1-17 of the present application are considered to involve an inventive step and subsequently fulfil the criterion set forth in Article 33(3) PCT.

D1 is considered the closest prior art in terms of technical features. It discloses compositions comprising 50En% of lipids, 18En% proteins and 32En% carbohydrates. Pantothenic acid is disclosed as being present at a dosage of **13.2mg**. The compositions are especially useful for oncologic patients showing weight loss and for reducing feelings of loss of appetite.

The differences of the application with respect to the closest state of the art D1 formulated in terms of Technical Features is the presence of a higher dose (14-1000mg) of pantothenic acid.
The alleged effect of this is stimulation of appetite.

Therefore the problem to be solved may be regarded as "providing an alternative composition for stimulating appetite".

Starting from D1, it is not obvious from its teaching that calcium pantothenate is used as the main appetite stimulant but rather as a vitamin and general nutritional component. In fact, emphasis in D1 is placed upon the fat content of the composition in order to treat the patient.

None of the remaining prior art documents disclose **together** that (i) calcium pantothenate is an appetite stimulant **and** that (ii) amounts of at least 14mg should be used.

D2 discloses that B vitamins stimulate appetite and suggests a preferred amount of 180 mg, however this is directed to treatment of **cows** not humans. Likewise D7 and D9 are directed to the use of pantothenic acid for treating pigs and fish respectively.
D4 discloses a vitamin preparation that contains 20-80 mg calcium pantothenate but does not suggest its direct action as an appetite stimulant.
D12 suggests a vitamin B deficiency can cause anorexia but no hint is given to the amount of vitamin B to be administered to overcome the deficiency.

Thus in principle the present application meets the criteria of Article 33(1) PCT, because the subject-matter of claims 1-17 involve an inventive step in the sense of Article 33(3) PCT.

Re Item VIII

Certain observations on the international application

1. The use the term "equivalent" in claims 1 and 11 should be avoided because it does not appear to have a precise meaning, thus rendering the scope of the claims unclear (Article 6 PCT) since it is not clear which specific compounds are encompassed by this term.

Claims

1. Composition for stimulating appetite in humans comprising in a daily dosage form 14 - 1000 mg pantothenic acid or an equivalent thereof, which equivalent comprises an equimolar amount of at least 14 mg pantothenic acid, and at least 15 En% proteins (or hydrolysed proteins or amino acids) and/or at least 32 En% carbohydrates and/or at least 18 En% lipids and said composition having a caloric value of at least 100 kcal per daily dosage.

2. Composition according to claim 1 wherein the proteins are selected from proteins from the group consisting of plants, vegetables, cereals, seeds, or whey, preferably from acidic whey.

3. Composition according to claim 1 or 2 wherein the composition comprises proteins that provides per 100 g amino acids at least one selected from the group consisting of 1.8-6 g methionine, 5.8-12.0 g lysine, is 1.5-4.0 g tryptophan and at least 8.0 g leucine.

4. Composition according to any of the preceding claims, wherein the serine/glycine ratio is 3.4 or higher.

5. Composition according to any of the preceding claims, comprising per daily dose at least one component selected from the group consisting of 0.2-5 g cysteine or one or more cysteine equivalents, 0.2-5 g nucleotide or one or more nucleotide equivalents (1-10 g yeast, cytidine, uridine, nucleosides), 0.1-5 g beta-alanine (only if the equivalent of pantothenic acid is (R)-pantoate), 300-3000 mg folic acid or one or more folic acid equivalents and 0.5-50 mg vitamin B6 or one or more vitamin B6 equivalents, 0,5 g of at least one selected from choline, betaine, dimethylglycine and sarcosine.

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6. Composition according to any of the preceding claims, said composition having a caloric value of at least 600 kcal, preferably at least 900 kcal, more preferably at least 1200 kcal per daily dosage.

7. Composition according to any of the preceding claims, comprising lipids in an amount of at least 1.5 g per 100 g composition, preferably in the range of 2.0-10 g, more preferably in the range of 2.7-8 g per 100 g composition.

8. Composition according to claim 7 wherein the amount of lipids comprises at least 12 g saturated fatty acids per 100 g lipids, preferably 14-50 g per 100 g fatty acids.

9. Composition according to claim 7 or 8 wherein the amount of lipids comprises at least 4.0 g myristic acid per 100 g fatty acids.

10. Composition according to any of the preceding claims, comprising at least 15 En% proteins (or hydrolysed proteins or amino acids) and at least 25 En% lipids and at least 40 En% carbohydrates.

11. Use of proteins (or hydrolysed proteins or amino acids) and pantothenic acid or an equivalent thereof for the manufacture of a composition that comprises at least 15 En% proteins (or hydrolysed proteins or amino acids) and that comprises in a daily dosage at least 14 mg pantothenic acid or an equivalent thereof, which equivalent comprises an equimolar amount of at least 14 mg pantothenic acid, for use in a method for stimulating appetite in humans.

12. Use according to claim 11 in which said method comprises the stabilisation and/or increase of body weight.

13. Use according to claim 11 or 12 in which said method comprises administration of a composition comprising a daily dose of pantothenic acid or an equivalent thereof of 14 - 1000 mg.

AMENDED SHEET

14. Use according to any of claims 11-13 in which said pantothenic acid or an equivalent thereof is selected from the group consisting of pantothenol, (R)-panto ate or salts or esters thereof, pantothenic acid or salts or esters or ethers thereof, pantetheine or esters or ethers thereof and coenzyme A, preferably pantothenol, (R)-pantoate or salts or esters thereof and pantetheine or esters or salts thereof.

15. Use according to any of claims 11-14 in a method for the treatment of patients suffering from infections, serious liver, kidney or heart disease, cancer of any kind, intestinal obstruction, inflammatory bowel disease, pancreatitis, irritable bowel syndrome, appendicitis, endocrine problems, diabetes, hypothyroidism, autoimmune diseases or disorders, psychological conditions, eating disorders, negative effects of medications or drugs, chemotherapy medications, alcohol, narcotics, antibiotics, diabetes medication, dementia, lung diseases, lung emphysema; traumata following surgery.

16. Use according to any of claims 11-14 in a method to treat nausea during pregnancy.

17. Use of a composition according to any of claims 1-10 for the use according to any of claims 11-16.

AMENDED SHEET